

Safe and Effective Opioid Prescribing in the Internet Age

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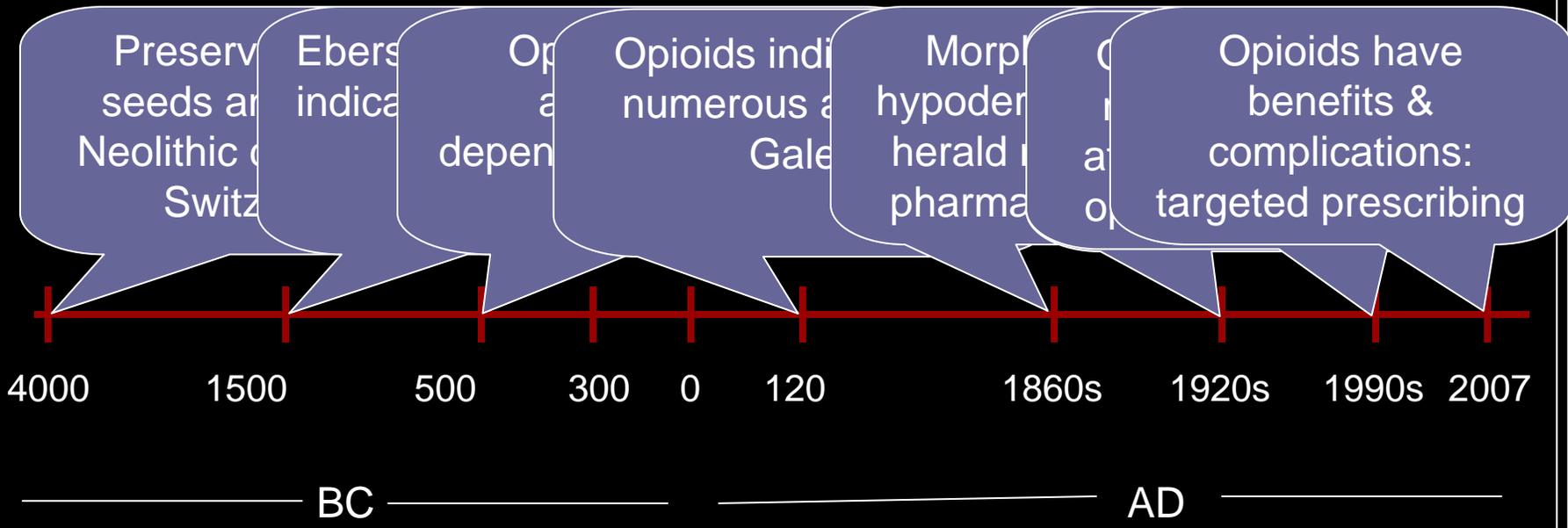
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“The dogmas of our quiet past are inadequate to our stormy present.”

Abraham Lincoln
State of the Union Address
December 8, 1863

Opioid Dogmas: Historical Timeline



Opioid Efficacy in Chronic Pain

- About 30 published placebo-controlled RCTs of opioids in chronic noncancer pain
 - All opioids tested work
 - All pain syndromes tested are relieved
 - Opioids more efficacious than comparators
- Case series show long-term safety and efficacy in a subgroup
- No long-term prospective studies

Opioid Tolerance

“It is important to note that while the concept of opioid “analgesic tolerance” has become accepted clinical dogma, development of opioid analgesic tolerance has never been truly assessed in a prospective, long-term controlled fashion in chronic non-cancer pain patients.”

Galer B, et al, Pain, 2005

Prospective study of elicited opioid side effects

Adverse Effect	Value (%) for Indicated Group			
	Total (N = 36)	No Opioid (N = 12)	Set Dose (N = 13)	Titrated Dose (N = 11)
Dry mouth	26.1	19.3	26.0	34.7
Drowsiness	24.1	14.6	22.1	36.9
Headache	22.1	15.1	20.2	31.8
Constipation	19.1	10.4	17.8	30.1
Nausea	16.2	4.7	13.9	31.3
Itching	12.9	8.9	14.9	14.8
Dizziness	11.6	9.4	18.8	5.7
Sweating	6.8	6.8	9.6	3.4
Weakness	6.3	5.7	7.7	5.1
Sneezing	2.0	1.0	1.0	4.0
Muddled thinking	1.6	3.1	1.4	.0
Nightmares	1.2	1.0	1.0	1.7
Heart palpitation	.7	.5	.0	1.7
Visual distortions	.7	.0	1.9	.0
Memory lapse	.5	1.6	.0	.0

Note: Wilcoxon matched-pairs signed-ranks test: No opioid vs. set dose, $z = -15.7$; $P < 0.001$. Set dose vs. titrated dose, $z = -16.8$; $P < 0.001$. No opioid vs. titrated dose, $z = -18.0$; $P < 0.001$.

Opioid hypogonadism: the major toxicity of long-term opioid therapy

- Daniell H, J Pain, 2002
 - 54 pts on opioid tx compared to 27 controls
 - 74% of pts had subnormal total testo levels
- Rajagopal A, J Pain Sympt Manage, 2003
 - 20 disease-free cancer survivors on opioids
 - Median testosterone 140 ng/ml (241-827)
- Rajagopal A, Pain, 2004
 - 20 cancer survivors on opioids vs. 20 not on opioids
 - 90% of opioid pts had hypogonadism vs. 40% controls
 - Sexual function, mood, fatigue, and QOL reduced
- Katz N (unpublished)
 - 25 pain pts on chronic opioids vs. 198 healthy controls
 - Testosterone subnormal in 68% of controls
 - All commonly used opioids implicated including methadone and TD fentanyl
- Six studies show high prevalence of hypogonadism on IT opioids
- At least four studies of methadone maintenance show hypogonadism with various control groups

The Dogma of Distinct Populations

“Good” pain patients
who “rarely” become
addicted to
prescription opioids

“Bad” people (non-
patients) who somehow
obtain opioids and
become addicted

The Dogma of Distinct Populations

Patients who use
opioids responsibly
over time

**PTS WITH
CO-MORBID
PAIN AND
SUBSTANCE
ABUSE**

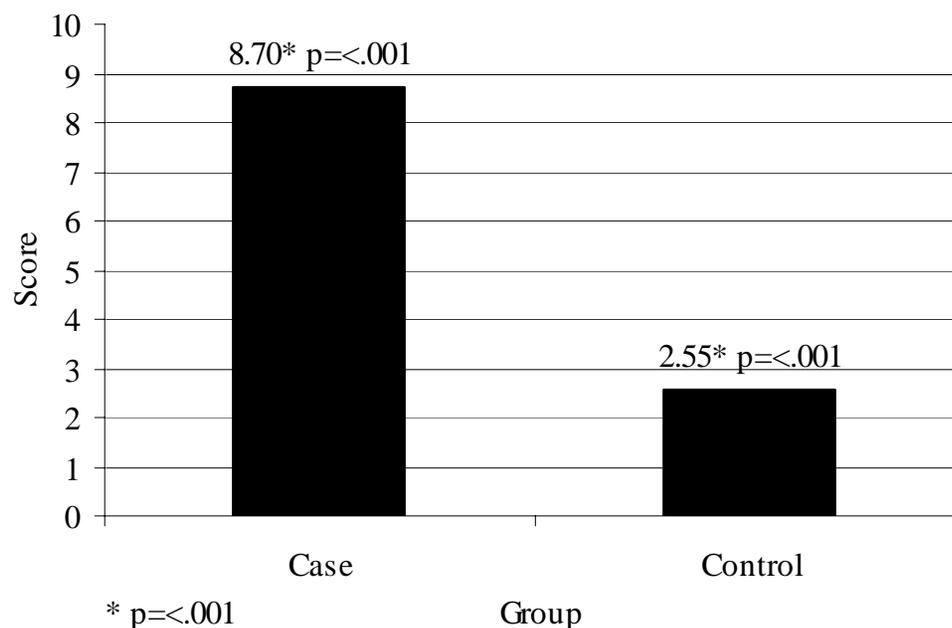
Non-patients who
obtain opioids and
become addicted

Co-Morbid Chronic Pain and Substance Abuse are Highly Prevalent

- 10-30% of adult population has chronic pain
 - ~10% background rate of substance abuse
 - 2-9 million in US with pain & SUD
- 1.5-2 million adults have opioid addiction
 - 30-60% of opioid addicts have chronic pain
 - 0.6-1.2 million with pain and opioid addiction
- 6-8 million in US on long-term opioids for pain
 - 20% positive urine tox
 - 1 million in US on opioid tx with pos. urine tox

Dogma: Patients prescribed opioids for pain do not develop euphoria

Figure 1: Mean Score of the Modified 46 Item ARCI MBG Subscale between Cases and Controls



n=40

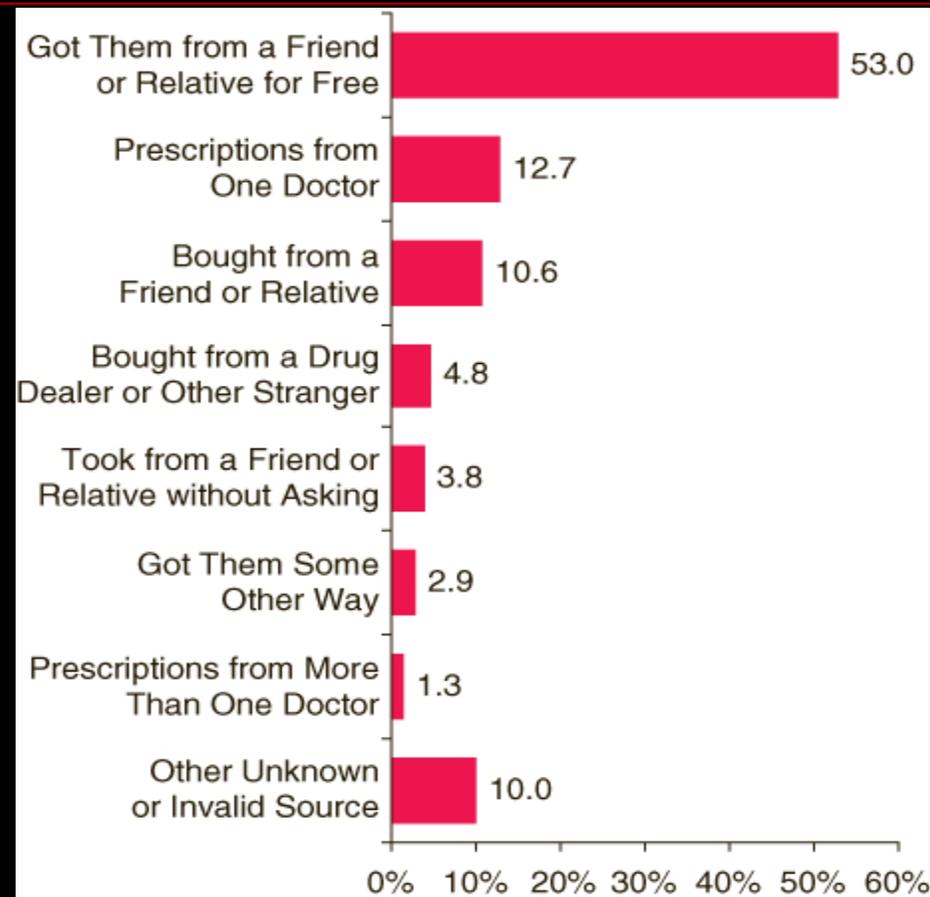
Prospective studies on the incidence of prescription opioid abuse among pain patients

- Adams E, et al, J Pain Symppt Manage, 2006
 - Prospective RCT, N=11,352
 - “Abuse Index” positive in: 2.5% for NSAIDs, 2.7% for tramadol, and 4.9% for hydrocodone
- Ives TJ, BMC Health Svcs Res, 2006
 - Prospective observational study, N=196
 - 32% incidence of “opioid misuse”

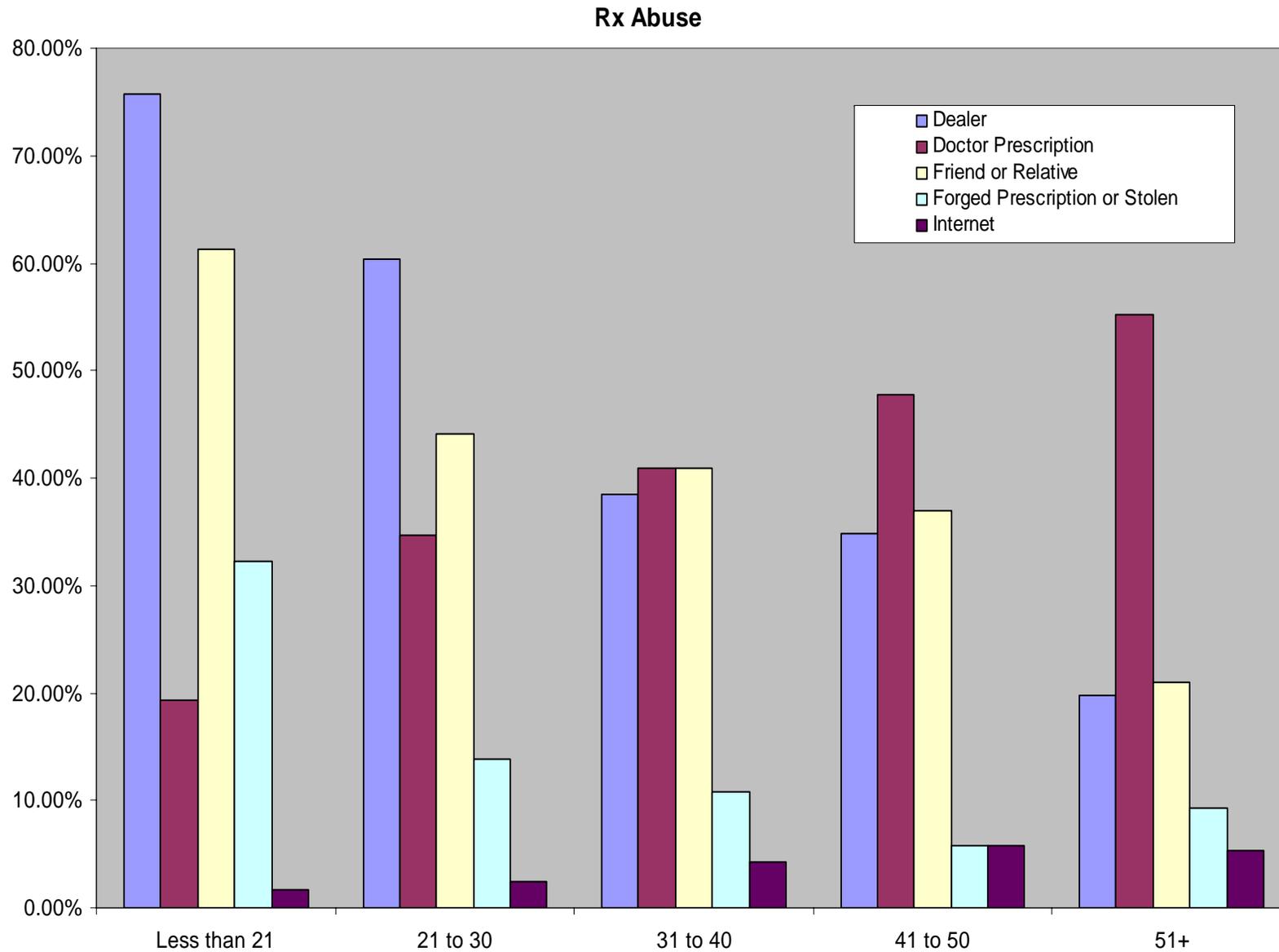
Volume of Diverted Opioids Study

- Opioids dispensed per year in US (IMS, 2002-2003)
 - 190 million prescriptions
 - 9.4 billion doses
- Non-medical users in last year (NSDUH)
 - 11 million people
 - 430 million non-medical use days
- Minimum of 430 million abused doses (1 dose/day)

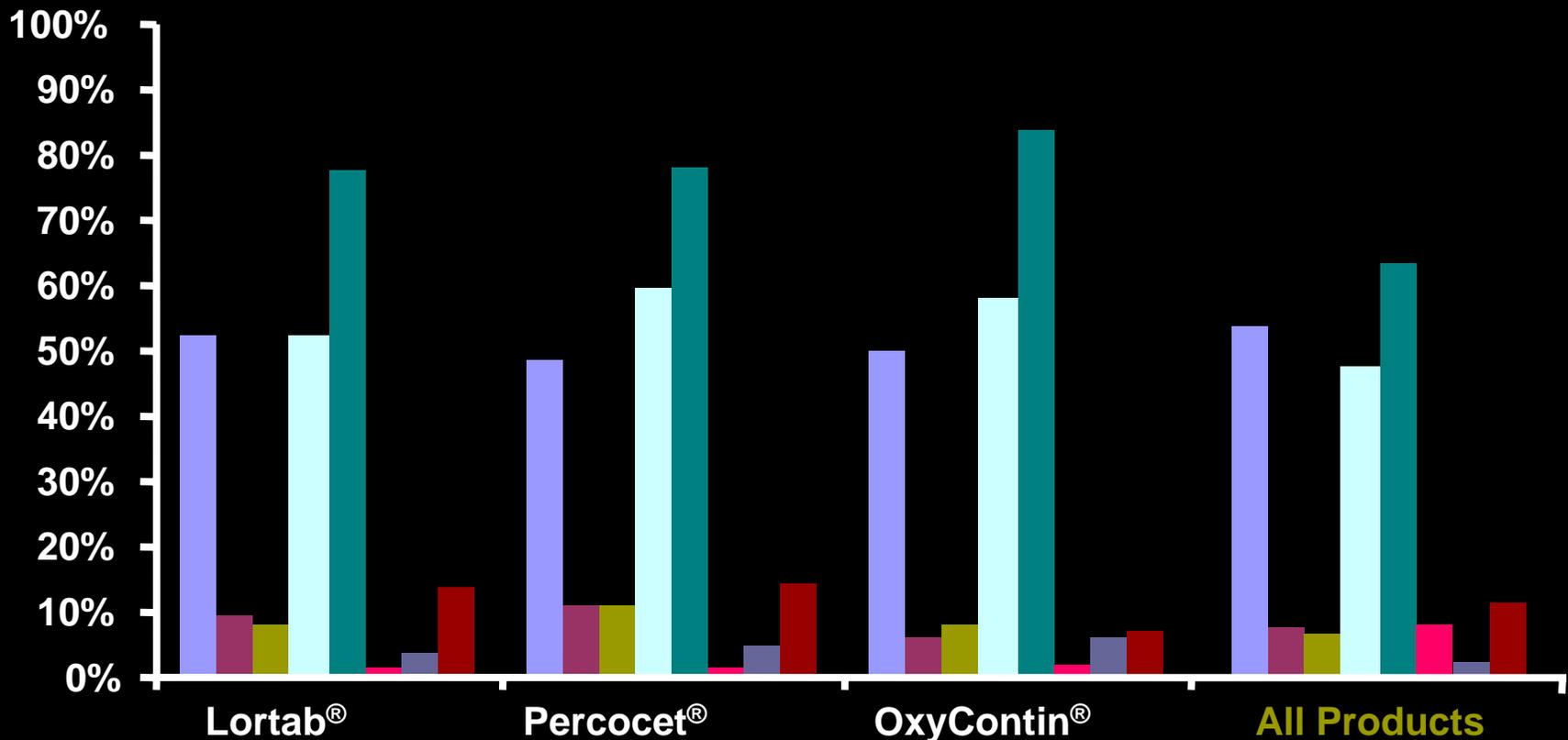
Figure 1. Percentages of Reported Method** of Obtaining Prescription Pain Relievers for Their Most Recent Nonmedical Use in the Past Year among Persons Aged 18 to 25: 2005 NSDUH



RADARS Diversion Study, Cicero T, et al, 2006



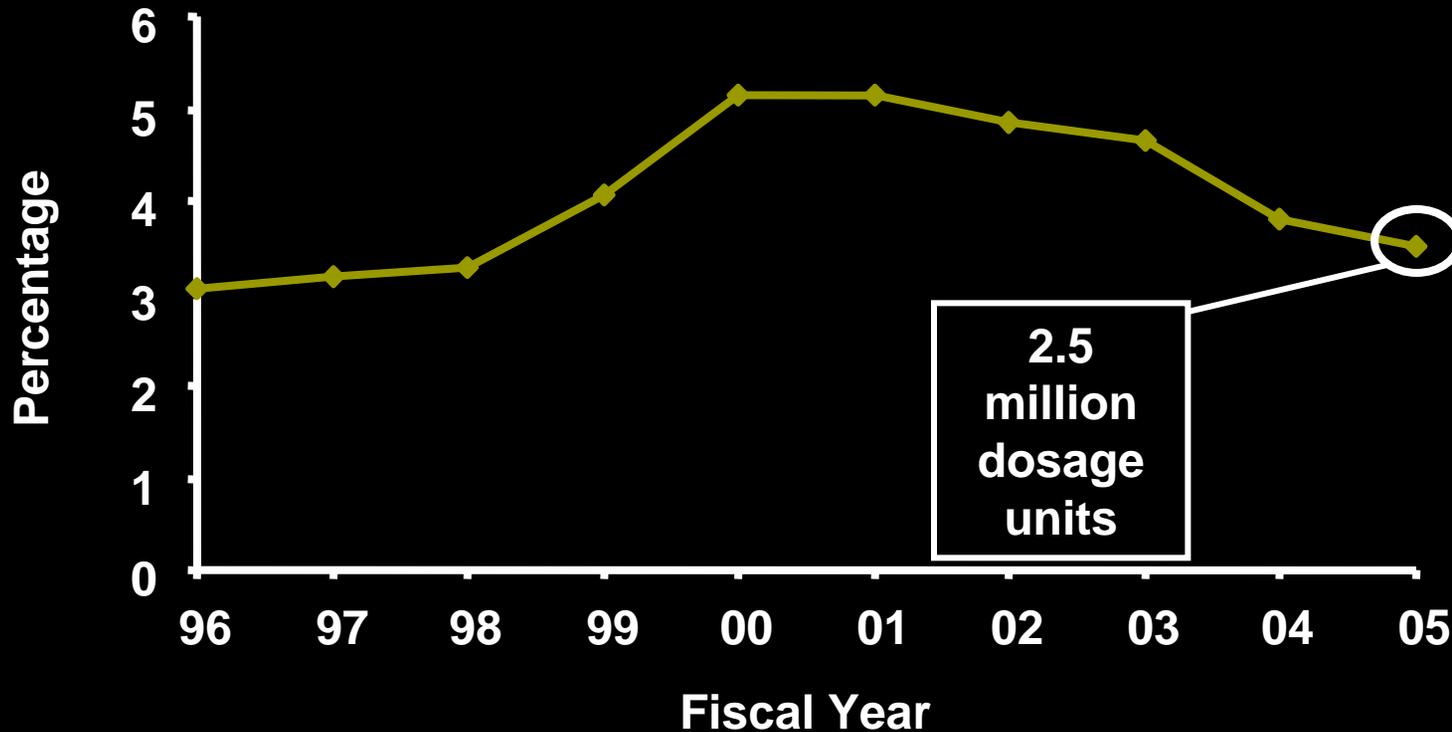
Source of Drugs (NAVIPPRO)



■ Own Prescription
 ■ Multiple Drs
 ■ Internet
 ■ Family/Friends
 ■ Dealer
 ■ Forgery
 ■ Stolen
 ■ Other Source

Inflexxion, Inc., 2006, data on file

Estimated Percentage of Schedule II Opioid Prescriptions Dispensed to Individuals Showing Questionable Activity* by Fiscal Year



*Questionable Activity = obtained Schedule II opioid prescriptions from ≥ 4 pharmacies and ≥ 4 physicians during the specified year

Role of the internet

■ Negative

- Source of diverted prescription opioids
- Encouragement of abuse
- Sharing of extraction recipes

■ Positive

- Harm reduction
- Opportunities for surveillance
- Opportunities for studies

Sample Internet Recipe

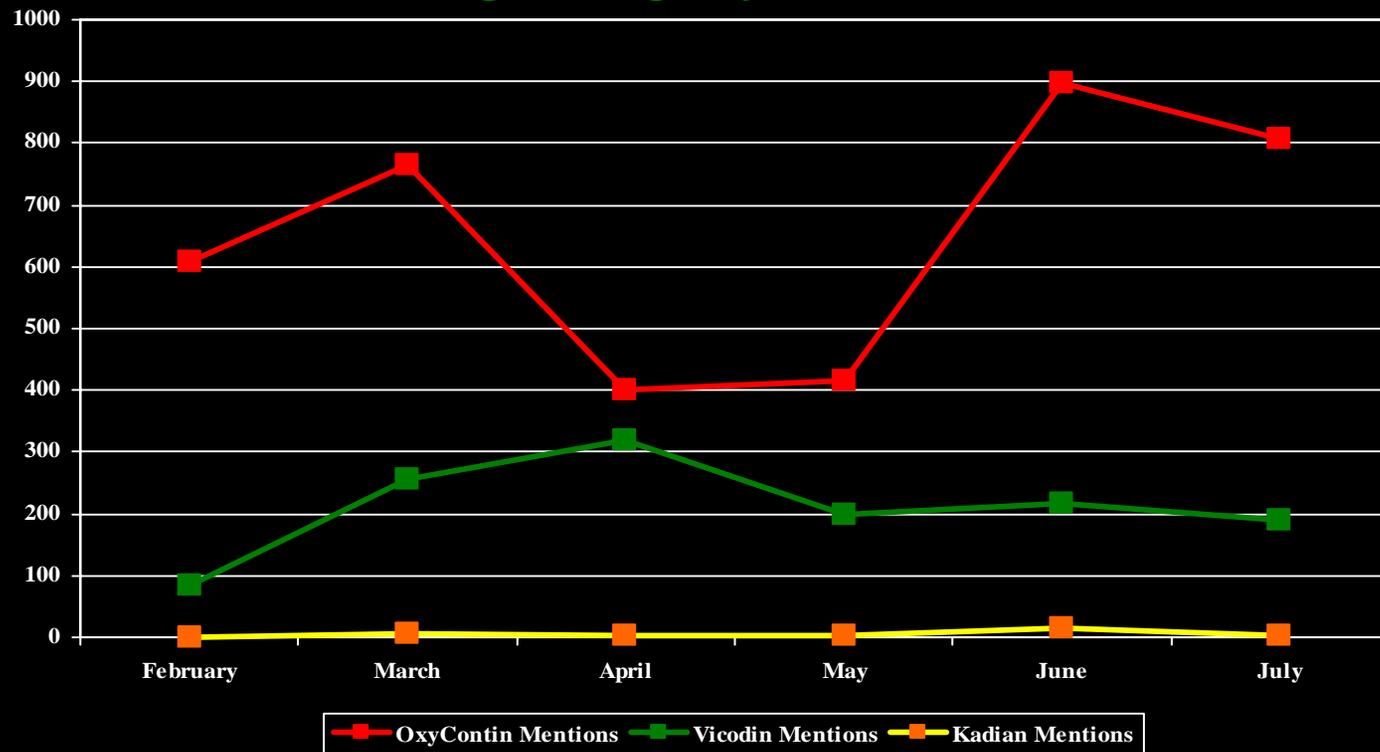
12/20/2006: If yer sloppy, like me, and in a hurry, like me, and don't have anything prepared, like me....I pour*3* contents of capsules into a spoon, crush'em up as good as I can w/another spoon, or whatever's hard and handy, (being careful not to have'em fly everywhere, I actually crush'em underneath a piece of paper, then scrape paper into spoon)then put a lot of water in, about two-three times what I actually want to fix, then stir'em up some more, 'til I got good milky solution, take little piece of balled up cotton, wet it in water, then throw in, suck up about 3/4 of a cc, whatever looks right, then fix.
Make sure what's left of this shitpile has at least 1cc of water left in it, hide spoon, stir, pound some more w/little plastic cap from end of rig, do this every few hrs until next day, or I just can't wait no more, then suck it up again. I got 3 pretty good rides out of this. On third one, this morning, I ate what was left. Still feel good...

Quantitative Internet Surveillance

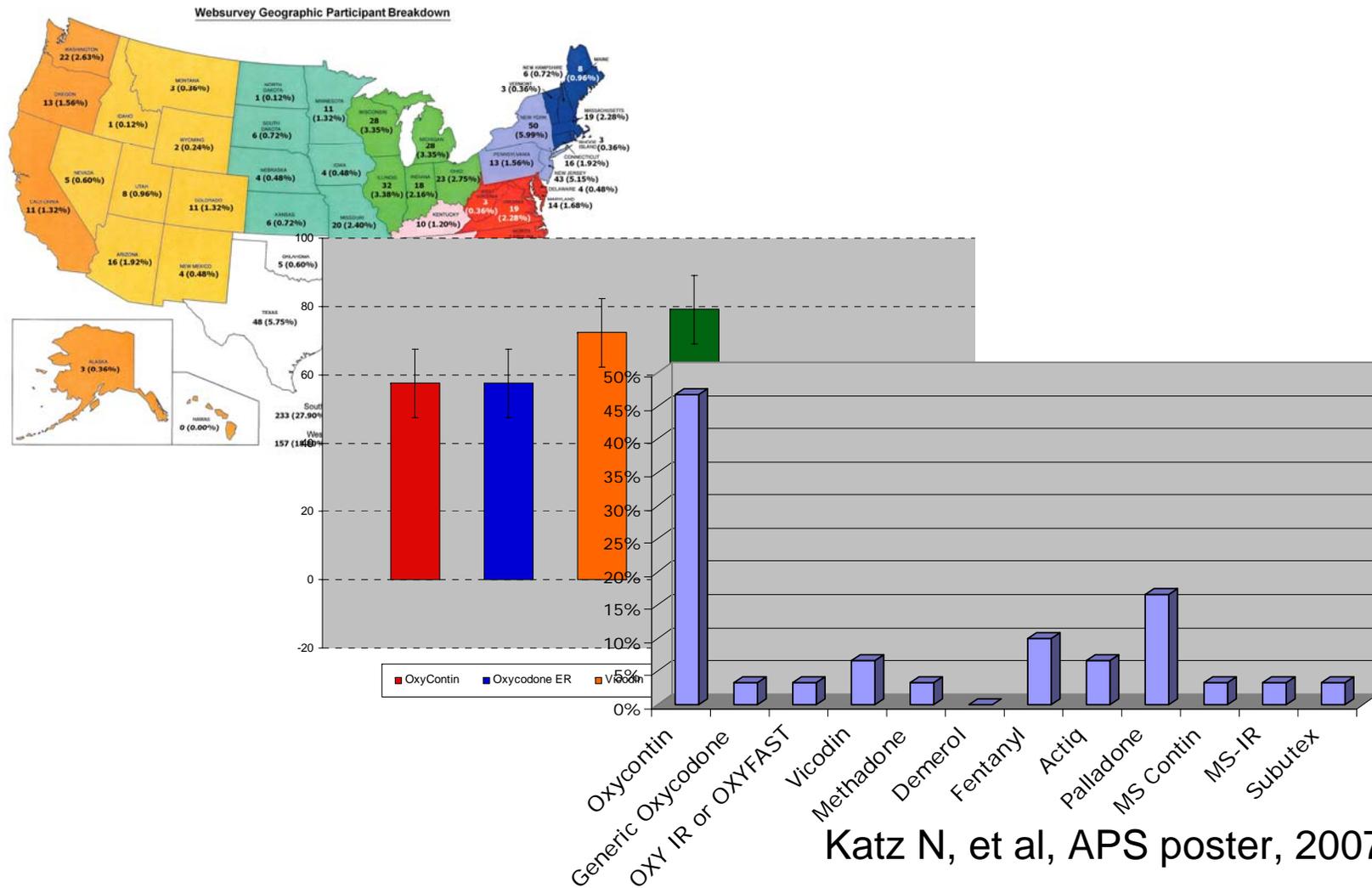
- Three internet message boards surveilled over six months
- Development and validation of rating system for drug-related posts
- N = 48,293 internet posts manually harvested
- Webcrawler currently continuously monitoring prescription opioid abuse mentions

Quantitative Internet Surveillance

Figure 4. Total Mentions of Target Drugs by Month



Internet survey of prescription opioid abuse, N=1033



Safe opioid prescribing in the “Internet Era”

- Triage
- Structured monitoring and documentation for all patients
- Single prescriber and pharmacy
- Treatment agreements
- Secure medication storage
- Urine toxicology
- PMP data
- Conviction/DUI data
- Significant other interviews
- Tamper-proof prescriptions
- Brief intervention and referral
- Exit strategy
- Abuse-deterrent opioids

Research agenda for safe opioid prescribing: “the anti-dogma”

- Large prospective study of opioid efficacy and incidence of and risk factors for prescription opioid abuse
- Validation of treatment matching of pain patients by risk category
- Validation of exit strategies
- Dissemination and validation of simple prescribing guidelines
- Validation of guidelines for interpretation of PMP data
- Validation of screening and assessment tools for POA
- Skill development training for SBIRT
- Training of pain physicians on addiction medicine
- Development of consumer education materials regarding responsibilities with opioids
- Clinical trials of treatment for patients with co-morbid pain and substance abuse

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Discussion

